MICRODISPERSION TREATMENT OF A PROTEIN OR PHARMACEUTICAL

FIELD OF THE INVENTION

The present invention relates generally to the inactivation of microorganisms utilizing radiation pulses, and more particularly to the treatment of a microdispersion of biologic or other pharmaceutical materials using high-intensity pulses of broad-spectrum light.

BACKGROUND OF THE INVENTION

Significant research has been directed at developing systems for treating labile biologic and small molecule organic pharmaceuticals for the purpose of inactivating contaminating microorganisms. A particular need exists for methods and apparatuses for sterilizing or reducing the microbiological contamination in proteins, small molecule organic pharmaceuticals and other materials vulnerable to microbial contamination without damaging the material.

One approach to the problem of microbiological inactivation has been directed to aseptic packaging technology for packaging of sterilized materials in sterile packaging materials, in order to achieve materials free of microbial contamination and having an extended shelf life. However, such methods and apparatuses have various disadvantages, such as requiring the extensive use of chemical disinfectants, which may leave residual chemical contaminants in the material and in some cases may lead to destruction of the biochemically labile material itself.

Another system for treating such biochemically labile materials utilizes microbiocides and microbiostats to prevent the growth of microbiological contaminants. However, recently such microbiocides and microbiostats have come under increased scrutiny by various governmental agencies, and in some cases have been shown to be potential human carcinogens. As a result, several microbiocides and microbiostats that were once commonly applied to the surface of products in order to prolong the shelf-life of the products have been or could be banned by governmental agencies.

Recently the photobiological effects of a broad-spectrum of light based techniques, have been studied. See, e.g., U.S. Pat. Nos. 4,871,559; 4,910,942; and 5,034,235, issued to Dunn et al. (hereinafter, the '559, '942, and '235 patents, respectively), all of which are incorporated herein by reference. However, these

efforts have been principally employed to inactivate microorganisms on food products or in containers for food products.

For example, an aseptic packaging system in combination with a photobiological food treatment apparatus has been developed and reported in the '559 patent, which utilizes short pulses of incoherent, broad spectrum light to preserve food products against microbial degradative processes. This system is stated to provide significant shelf-life and stability enhancements to the food product. Application of pulses of high-intensity, incoherent polychromatic light is also stated to provide efficient, effective, high throughput processing and result in many practical and economic advantages. Moreover, the short duration and the spectral range of each pulse is asserted to permit spatial localization of various of the preservative effects of the light pulses to a thin surface layer such as the surface of the food product or packaging material.

Other studies of the photobiological effects of light are reported in Jagger, J., "Introduction to Research in Ultraviolet Photobiology", Prentice Hall, Inc., 1967. U.S. Pat. No. 2,072,417 describes illuminating substances, e.g., milk, with active rays, such as ultraviolet rays; U.S. Pat. No. 3,817,703 describes sterilization of light-transmissive material using pulsed laser light; and U.S. Pat. No. 3,941,670 describes a method of sterilizing materials, including foodstuffs, by exposing the materials to laser illumination to inactivate microorganisms.

While these systems have proven very effective at treating food products, these systems are generally not applicable to highly labile, potentially microbially contaminated materials, such as proteins and other pharmaceuticals, which can be easily denatured or destroyed by prolonged exposure to the irradiation source. For example, two apparatuses for purifying biological materials utilizing a broad-band light source are described in the '599 patent: a static platform technique in which the sample is placed on a platform or in a container subject to irradiation; and a flow system in which the sample is flowed through a transparent tube, which is itself subject to an irradiation source. However, both of these systems have the disadvantage that the portion of the sample on the wall of the platform or flow-tube is subject to a much greater irradiation intensity than the portion of the internal bulk of the sample. In order to provide sufficient irradiation to effectively decontaminate the entire sample, these boundary regions may be subject to

sufficient irradiation to denature or destroy very sensitive biological materials such as proteins or other substances, such as small-molecule organic pharmaceuticals.

Accordingly, there is a need for a system and method of safely and non-destructively treating irradiation-sensitive biochemically labile materials utilizing short-pulses of energetic emissions without the problems of flow-through cells, cell boundary layer effects, cell material energy absorption effects and sample geometry absorption effects that arise from conventional flow-through treatment cells.

SUMMARY OF THE INVENTION

The present invention is directed generally to a device and method for inactivating microorganisms without significant damage to the sensitive biologic or other organic materials, and more particularly for inactivating microorganisms by subjecting a microdispersion of biological or other pharmaceutical material to short-duration, high-intensity pulses of an energetic emission.

In one embodiment, the invention is directed to an apparatus for inactivating microorganisms in a biological or other pharmaceutical material comprising a flashlamp; a power supply coupled to the flashlamp; a flow chamber designed to produce a microdispersion of the material across an exposure region such that the material is exposed to high-intensity, short-duration pulses of broad-spectrum polychromatic light emitted from the flashlamp, in such a manner that the light destroys microorganisms without damaging the biologic or other pharmaceutical material.

In another embodiment, the flow chamber comprises at least one needle designed and arranged to non-destructively create droplets of the biological or other pharmaceutical material having a substantially uniform size at a substantially uniform rate. In such an embodiment, the droplets created are preferably less than 3 mm in diameter.

In yet another embodiment, the flow chamber further comprises at least one gas nozzle designed to produce a flow of gas along the edges of the flow chamber such that droplets are urged away from the wall by the gas flow. In a preferred embodiment, a chemically inert gas is utilized in the gas flow, such as a noble gas.

In still another embodiment, a droplet retarder is provided such that the rate of fall of the droplets through the flow chamber can be controlled. In one preferred embodiment, the retarder takes the form of an upwardly directed flow of gas. In

another preferred embodiment, the retarder is a pair of charged plates designed to adjustably retard the rate of fall of the droplets.

In still yet another embodiment, the flash lamp is designed to emit multiple flashes in a time period such that a droplet falling through the exposure region of the flow chamber is irradiated multiple times. In one such embodiment, a single strobe lamp is utilized. In another such embodiment, a plurality of lamps timed to sequentially emit are utilized. In still another such embodiment, the flash lamp emits in both the ultraviolet and the visible spectra.

In still yet another embodiment, the droplets are collected and any flow gas is removed in a collection chamber positioned at the exit of the flow chamber. In one such embodiment, the droplets are collected on a surface having a low energy coating such as teflon.

In still yet another embodiment, the flow chamber and the collection chamber are temperature controlled to maintain a constant temperature.

In still yet another embodiment, the invention is directed to a method of irradiation treating a microbiologically labile material. The method comprising running a labile biologic or other pharmaceutical material through the microdispersion treatment apparatus described above.

BRIEF DESCRIPTION OF THE DRAWINGS

The above and other aspects, features and advantages of the present invention will be more apparent from the following more particular description thereof, presented in conjunction with the following drawings wherein:

FIG. 1 is a schematic illustration of one embodiment of an irradiation microdispersion treatment device according to this invention;

FIG. 2 is a schematic illustration of one embodiment of a microdispersion flow chamber according to this invention; and

FIG. 3 is a flow diagram of a process for manufacturing a purified labile biologic or other pharmaceutical material utilizing the irradiation microdispersion treatment device according to this invention.

Corresponding reference characters indicate corresponding components throughout the several views of the drawings.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed to a treatment device and method to non-destructively purify a flow of labile biologic or other pharmaceutical material utilizing an energetic emission without subjecting the sample to the boundary effects inherent in conventional flow cells. It should be understood that the "flow" of material utilized by the current invention refers to a flow or dispersion of small discrete droplets or spheres of the labile biologic or other pharmaceutical material, not a continuous forceful emission, both of which may be encompassed by the general term "spray," but only the former of which is desired herein, and that such flow is referred to herein as a "microdispersion" and the apparatus as a "microdispersion treatment device."

Referring to FIG. 1, a schematic view is shown of an embodiment of an apparatus for the treatment of labile biologic or other pharmaceutical materials such as proteins, genetic materials and pharmaceuticals by exposing a microdispersion of the material to high-intensity, short-duration pulses of an energetic emission. In the embodiment shown in FIG. 1, the microdispersion treatment device **10** comprises an energetic source **12** for emitting an energetic emission **14**; an enclosure defining a treatment chamber **16** having an inlet **16a** and an outlet **16b** through which a microdispersion of the product **18** flows and interacts with the emission **14**; a second enclosure defining a pretreatment chamber **20** in fluid communication with the inlet **16a** of the treatment chamber **16**; and a third enclosure defining a collection chamber **22** in fluid communication with the outlet **16b** of the treatment chamber **16**.

In the embodiment shown in FIG. 1, the pretreatment chamber **20** comprises a chamber having a plurality of nozzles **24** defining a fluid conduit between the pretreatment chamber **20** and the treatment chamber inlet **16a**. In the embodiment shown in FIG. 1, the nozzles **24** are designed such that the product **18** is delivered therefrom into the treatment chamber **16** in the form of a plurality of droplets **26**. Any suitable nozzle **24** design may be utilized in the embodiment shown in FIG. 1 such that the droplets **26** are produced without the use of excess shear forces which might damage the material **18**, and such that the droplets **26** have a diameter that allows complete penetration of the emission **14** to all droplets **26**. For example, the nozzles **24** may comprise a plurality of needles suitably gauged such that the material **18** passes therethrough undamaged. In such an embodiment, it will be

understood that the gauge of the needle **24** will depend on the nature of the material to be treated. For example, in a treatment in which the material **18** is an immunoglobulin solution, a large diameter 14 to 20 gauge needle **24** would impart only insubstantial shear forces on the immunoglobulin solution passing therethrough, however, a narrower 30 gauge needle **24** would produce large shear forces and cause substantial damage to the immunoglobulin as the material was forced through the narrow needle shaft. Suitable nozzle diameters are known or easily determined experimentally for any material through conventional strain test assays known in the art.

Although conventional drip nozzles **24** are shown in the embodiment shown in FIG. 1 and described above, any device suitable for non-destructively producing a mist of droplets **26** containing the product **14**, and having a diameter suitable for treatment may be utilized in the microdispersion treatment device **10** of the current invention. As discussed above, the droplet formation device **24** chosen has only two requirements: 1) that the chosen method be compatible with the material **18**, such that the material is not decomposed, denatured or otherwise damaged by the misting process; and 2) that the diameter of the droplets **26** themselves be suitable for treatment, *i.e*, such that the emission **14** is capable of sufficiently energizing the entire droplet **26**.

Under the first requirement, the method of producing the droplets **26** must be compatible with the material **18** such that the material **18** is not substantially damaged. For example, many labile biological products, such as proteins, are sensitive to shear force and heat. Thus, in an embodiment in which the material **18** to be treated is protein, a droplet device **24** having a low shear force and low heat input should be utilized, *e.g.*, a standard gravity needle drip mechanism as described above or a water-fall mechanism. Likewise, pressurized sources or foaming agents which create large physical and chemical shear forces would not be suitable for such sensitive materials. Generally, materials **18** comprising long chains or materials with a large number of subunits are more easily damaged by shear forces and/or other physical stresses. Techniques suitable for any chosen material **18** are known in the art or are easily determined experimentally via conventional strain test assays.

Under the second requirement, a suitable diameter for the droplets **26** in the device **10** of the invention is one which allows the transmittance of sufficient

emission energy through the droplet **26** to inactivate any microbial contaminants in the material **18**. A suitable droplet **26** diameter will depend on the concentration of the material **18** and the inherent transmittance of the material **18** to the emission **14** according to Beer's law:

$$I = I_0 e^{-k'cd} \qquad (1)$$

where "d" is equal to the thickness of the material **18** (droplet diameter), "c" equals the concentration of the material **18**, "k'" equals the absorption coefficient of the material at a specified emission wavelength and solution temperature, and I_0 equals the initial intensity of the emission **14**. According to Beer's law, then, a material having a higher absorption coefficient will require either a lower concentration of solution or a smaller diameter droplet **26** to ensure that the entire droplet **26** is sufficiently energized by the emission **14**. Materials such as air and water are relatively transparent to light, including significant portions of the UV spectrum. Accordingly, there is relatively little attenuation through absorption in such media, with the flux density decreasing largely only as a function of distance from the light source. However, for a material having significant absorption, flux density will decrease as a function both of distance from the emitter **12** and of product absorption. Indeed, it will be understood that it may be difficult to treat some highly absorbent materials and/or materials having highly absorbent additives, such as, dyes or detergents or highly scattering additives, such as undissolved particles, because the attenuation of the emission **14** would be too great to provide sufficient exposure to the entire volume for the material. In a preferred embodiment, the droplet diameter is equal to or less than about 3 mm, which corresponds to the utility limit for many treatable substances.

While the intensity of the light penetrating the entire droplet "I" must be sufficient to inactivate micorbial contaminants in the entire volume of the droplet, the level of intensity "sufficient" for the material **18** will depend on the level of inactivating emission energy required for the material and the nature of the material to be irradiated. Such values are either well known from prior studies of the photobiological effects of light or are easily determined experimentally via intensity/inactivation assays. Studies of the degree of efficacy and the required emission intensities have been determined for infrared light (780 to 2600 nm),

visible light (380 to 780 nm) and far ultraviolet light (170 to 200 nm). See, e.g., U.S. Patent Nos. 4,871,559; 4,910,942; and 5,034,235, issued to Dunn et al., all of which are incorporated herein by reference.

In a preferred embodiment of the present invention, the droplet formation device **24** is designed such that droplets **26** of substantially uniform diameter are formed at a substantially uniform rate. Having uniform droplets **26** formed at a uniform rate allows for more reproducible and controlled treatment regiments, i.e., emission intensity, pulse time and dwell time within the treatment chamber to be used reducing the anisotropy of the treatment of the material **18**.

Regardless of the technique utilized to form the droplets **26**, the droplets **26** thus formed are dripped through the treatment chamber inlet **16a** and into the treatment chamber **16** itself. Although the treatment chamber **16** is shown as a cylinder in the embodiment shown in FIG.1, any configuration suitable to allow the droplets **26** formed in the pretreatment chamber **20** to move therethrough and interact with the emission **14** impinging on the treatment chamber may be utilized. For example, in one embodiment, shown in FIG. 2, the treatment chamber **16** is rectangular such that the droplets **26** fall through the chamber in a single line, such that the emission **14** is unimpeded prior to impinging on each droplet **26**. Regardless of the specific geometry utilized, the dimensions of the treatment chamber **16** will vary depending upon many factors including: the absorption characteristics of the material **18** to be treated, the physical and operating characteristics of the emitter **12**, and the rate the material **18** moves through the treatment chamber **16** between pulses, i.e., flashes, of light. To enhance the intensity of the emission **14**, the treatment chamber **16** may include a reflector assembly **36** as its outer wall or as an external reflector, in order to reflect the emission **14** traversing the material **18** back into the chamber **16**.

The above discussion assumes that the material **18** is allowed to free-fall under the influence of gravity through the treatment chamber **16**. However, depending on the total emission exposure required to treat the material **18**, and the arrangement of the emission source **12** in relation to the treatment chamber **16**, it may be necessary to have an impractically long treatment chamber **16** to ensure that the residence time of the material **18** in the treatment chamber **16** is sufficient or to have an impractically or expensively large number of emitters **12** to ensure that the material **18** is exposed to sufficient energetic emission **14** for treatment.

In such cases, a flow controller **28** may be additionally provided in the treatment chamber **16** to control the flow rate of the material **18** through the treatment chamber **16** in relation to the pulse repetition rate of the emission source **12** so that during the residence time of the material **18** within the treatment chamber **16**, all of the material **18** is exposed to a predetermined level of emission, i.e., number of pulses, overall intensity of pulses, or overall exposure of material. Accordingly, the flow controller **28** ensures that the material **18** exiting the treatment chamber **16** is treated to a desired degree. In addition, a flow controller **28** ensures uniform transport of the droplets **26** decreasing the anisotropy of the treatment and yielding uniform and reproducible treatment regiments. Alternatively or in addition, the flow controller **28** may provide mixing to insure that all of the material **18** being treated is subjected to an appropriate flux intensity and number of pulses (for the desired degree, or level, of inactivation, i.e., kill or sterilization).

In one exemplary embodiment, shown in FIG. 2, the flow controller **28** comprises at least one gas nozzle designed and arranged to direct a flow of gas **30** upward through the treatment chamber **16** against the falling droplets **26** of material **18** such that the speed of the falling droplets **26** is retarded. In such an embodiment, any gas could be utilized such that the flow of gas **30** does not react with the material **18**. For example, suitable chemically inert gases include: argon, helium, neon and nitrogen. If a gas flow **30** is utilized, the gas may be scrubbed of material **18** prior to venting or recycling in the collection chamber by a variety of techniques including filtration, and/or condensation. Further if the gas from the gas flow **30** is to be recycled, it can be purified utilizing any known purification technique, such as, for example, filtration, incineration or irradiation.

Although a gas jet flow controller **28** is described above, any suitable flow controller may be utilized in the present invention. For example, the flow controller **28** may comprise a pair of charged plates designed and arranged to emit a retarding field to control the flow rate of the material **18**. In addition, although only retarding flow controllers **28** are discussed above, the flow controller **28** might comprise an accelerating field or gas flow to speed the flow of the droplets of material through the treatment chamber. Finally, although only flow controllers having a linear gravity induced geometry are described above, any suitable geometry of flow may be utilized such as, for example, a helical geometry, or a flow induced via a field or force directed in opposition to the force vector of gravity. The

only requirement for the flow controller **28** of the present invention is that the force exerted by the flow controller **28** must be of a level sufficient to adequately retard or accelerate the droplets **26** without denaturing or otherwise damaging the material **18** being treated.

To prevent droplets of the material **18** from adhering to the walls of the treatment chamber **16** and receiving an excessive dose of the emission **14**, the treatment chamber may also comprise a system for sweeping material **18** from the walls of the treatment chamber **16**. Such a sweeping device **32** system could comprise a plurality of gas nozzles, as shown in FIG. 2, designed and arranged to direct a curtain of gas **34** along the walls of the treatment chamber **16** such that any droplets **26** impinging on the walls are swept therefrom and into the outlet **16b** of the treatment chamber **16**. In such an embodiment, any gas could be utilized such that the gas **34** does not react with the material **18**. For example, suitable chemically inert gases include: argon, helium, neon and nitrogen. If a gas curtain **34** is utilized, the gas flow may be scrubbed of material **18** prior to venting or recycling in the collection chamber by a variety of techniques including filtration, and/or condensation. Further if the gas from the gas curtain **34** is to be recycled it can be purified utilizing any known purification technique, such as, for example, filtration, incineration or irradiation.

Although a gas curtain **34** is described in the exemplary embodiment above, any sweeping device **32** or other method suitable for minimizing droplets **26** impinging on the walls of the treatment chamber **16** may be utilized in the present invention. For example, a liquid or energetic emission curtain could be used in place of the gas curtain **34** to sweep the droplets **26** off the wall. Alternatively, the walls of the treatment chamber **16** might be coated with a substance that prevents droplets **26** from coalescing and adhering thereto. Likewise, the treatment chamber **16** may be made of any material suitable to allow sufficient transmission of the emission **14** therethrough. For example, glass may be utilized in visible light applications where glass is transparent to wavelengths in the visible spectrum (between about 380 and 780nm). However, in an embodiment in which the emission **14** utilizes the UV portion of the spectrum (between about 170 and 200nm), quartz or a similar material should be utilized which is transparent to UV light. Although only solid walled apparatuses are discussed above, it should be understood that any device suitable for containing the substance within the

treatment region may be utilized with the current invention, such as, for example, a containment gas curtain or powered field.

As discussed above, the emitter **12** shown in FIGs. 1 and 2 schematically, may comprise any suitable source of energizing emission capable of inactivating microbial contaminants in the material **18**. In one embodiment, the emitter **12** is a pulsed light source, such as those described in U.S. Patent Nos. 4,871,559; 4,910,942; 5,034,235; 5,658,530; and 5,900,211 issued to Dunn et al.; 5,768,853 and 6,013,918 issued to Bushnell et al.; and 5,925,885 issued to Clark et al., all of which are incorporated herein by reference. Typical operating parameters for a suitable light source are a flashlamp which emits an emission having a spectrum including wavelengths of at least about 170 to about 2,600nm, having pulses of duration between about 0.001 and about 100ms, and having an intensity between about 0.01 and about 50J/cm^2.

In such an embodiment, any pulsed light source emitter **12** may be utilized, such as, for example, a high powered Xenon flashlamp. If a flashlamp emitter **12** is utilized, the flashlamp may be constructed in nearly any shape; and similarly, if reflectors **36** are used in conjunction with the flashlamp emitter **12**, the reflectors may be made of many different materials in many different geometries to direct pulses of light from the flashlamps to the product to be treated. Suitable reflector designs may be found in "The Optical Design of Reflectors", Second Edition, William B. Elmer, Published by John Wiley and Sons, Inc., New York, which is incorporated herein by reference. In such an embodiment, the emitter source **12** may use one or a plurality of flashlamp emitters **12** and associated reflectors **36** to create high-intensity, short-duration pulses of incoherent polychromatic light in a broad spectrum in the treatment chamber **16** in which the material **18** to be treated is exposed to the emission **14**.

While the embodiment shown in FIG. 2 utilizes a plurality of individual straight flashlamp emitters **12** and reflector elements **36**, other arrangements may also be utilized. For example, one or more flashlamp emitters **12** may alternatively (or in addition) be located externally or internally in the treatment chamber**16**. A preferred design is shown in FIG. 2, in which the material **18** to be treated is conducted through a treatment chamber **16** made of a transparent material (e.g., a quartz tube). The treatment chamber **16** is positioned along one focus of an elliptical reflector **36** and a flashlamp emitter **12** is positioned along another focus

of the elliptical reflector **36**. If a plurality of emitters **12** are utilized, such emitters may all be illuminated simultaneously, may be illuminated in pairs, or may be illuminated serially. Preferably, however, the emitters **12** are illuminated simultaneously such that emissions **14** from adjacent emitters **12** cooperate at the boundaries between such emitters **12** in order to assure that a minimum total fluence is achieved over the entire area being treated, which enables the use of lower fluence levels per flash, while preserving a high overall fluence level and a high degree of material **18** treatment.

Although the embodiments of the present invention discussed above include many potential applications for the reduction of viable organism, microbe or virus numbers, or enzymatic activity in the treatment of biologically labile materials employing high-intensity, short-duration, broad-spectrum, polychromatic, incoherent pulses of light, any emission **14** suitable for the treatment, i.e., inactivation of unwanted microbial materials in a sample may be utilized, such as, for example, gamma rays or other energetic emissions. Further, where a light-based emission **14** is utilized, it is preferred to utilize a broad-spectrum output, including near and far ultraviolet light components of the spectrum, such that multiple inactivation pathways may be energized in the target material simultaneously and thereby relatively low fluences may be utilized. For example, even at very high organism densities (up to $1x10^6$ to $1x10^8$), only one or two flashes at an energy density of 0.4 or 0.5 J/cm^2 per flash (or as low as 0.1 J/cm^2, or even as low as 0.01 J/cm^2 or less, depending on the microorganisms to be inactivated) have been reported to result in inactivation, i.e., kill or sterilization or inactivation, of spores, vegetative bacteria, viruses, unwanted DNA and the like.

In any of the above embodiments, an emission-sensitive element (not shown) may be further incorporated into the treatment chamber **16** such that the intensity of the light reaching the droplets **26** is constantly monitored such that a indication of the effectiveness of the treatment can be constantly read-out. Further, the emission-sensitive element may further be connected through a closed-loop feedback control system to the emitter **12** such that if the intensity of the emission **14** impinging on the droplets **26** is insufficient or excessive, i.e., below or above a prescribed threshold, the power delivered to the emitter **12** and thus the intensity of the emission **14** may be increased or decreased accordingly.

The collection chamber **22** may comprise any receptacle suitable to catch and collect a significant proportion of the droplets **26**. In the embodiment shown in FIG. 1, the collection chamber comprises a funnel **38** disposed at the outlet **16b** of the treatment chamber **16** such that the droplets **26** passing through the treatment chamber **16** impact the sloped sides of the funnel **38** and are directed into the enclosure defining the collection chamber **22**. Although the collection chamber **22** shown in FIG. 1 is a simple vessel having no outlets, it should be understood that the collection chamber **22** could have any suitable outlet (valved or unvalved) such that the treated material **18** passing therein may be directed to any additional processing machinery. For materials **18** having low shear force thresholds, it may be necessary to coat the funnel **38** and/or the inner walls of the collection chamber **22** with a low energy material capable of reducing the impact force felt by the falling droplet. Any suitable low-energy material could be utilized which is inert to the material **18** and capable of being applied to the surfaces of the treatment device **10**, such as, for example, teflon, polycarbonate or polypropylene.

Additionally, a temperature controller (not shown) may be integrated into pretreatment chamber **20**, the treatment chamber **16** or the collection chamber **22** of the microdispersion treatment device **10** of the current invention to either heat or cool the material **18** before, during and/or after treatment to ensure that the material **18** is maintained at a temperature suitable for the material **18**.

The present invention is also directed to a method for treating a biologically labile material **18** utilizing the microdispersion treatment device **10** of the current invention. During operation, a material is introduced into the pretreatment chamber **20** from whence it is either gravity-drained or pressurized such that the material **18** is directed through the droplet formation device **24** and into the inlet **16a** of the treatment chamber **16** in the form of a microdispersion of droplets **26**.

The droplets **26** then in turn flow through the treatment chamber **16**. Simultaneously, the emitter **12** is energized to emit an emission **14** which passes into the treatment chamber **16** such that the emission **14** interacts with the droplets **26** of the material **18** passing therethrough. The droplets may be acted on by various forces to improve the treatment characteristics of the microdispersion treatment device **10**. For example, in an embodiment having flow controller **28** the droplets **26** may be retarded by an electric field or a gas flow **30** such that the flow

of the droplets **26** through the treatment chamber **16** is regulated. In addition in an embodiment having a wall sweeping device **32**, droplets **26** impinging on the walls of the treatment chamber **16** may be swept off the walls via a curtain **34** of gas directed thereagainst by the sweeping device **32**.

Once the droplets **26** pass through the treatment chamber **16** and out of the outlet **16b** they are collected via a collection device **38** and directed into the collection chamber **22** either for final packaging or for further treatment.

EXAMPLE 1

An exemplary embodiment of the treatment of a solution of 5% liquid immune globulin intravenous protein (IGI) utilizing the microdispersion treatment device and method is described below in relation to FIG. 3.

In this hypothetical embodiment, two alternative treatment pathways are shown. For either treatment pathway, Step (1) of the process would involve obtaining a precipitate (GGI-ppt) containing the IGI protein. In Step (2), the precipitate would then be material balanced for clarification. In the process including Step 2', the material balance would be conducted without any microdispersion treatment, while the process including Step 2" would run the material balanced IGI through the microdispersion treatment device **10** of the current invention to inactivate any unwanted contaminants. Steps 3, 4 and 5 of either of the processes would involve an OSD treatment followed by the adsorption and filtration of the material, then followed by a CM Sephadex wash, respectively. Step 6 involves a CM Sephadex elution. In the process including Step 6' the CM Sephadex elution would further involve running the IGI sample through the microdispersion treatment device **10** according to the present invention, while the process including Step 6", would have already treated the IGI sample by that point. Steps 7 to 10 in such an embodiment would then be identical for the two processes; the IGI would enter a post wash, followed by a pre-UF clarification, followed by an ultra-filtration, followed by the addition of Sorbitol and a pH adjustment, respectively. Finally, at Step 11 the material would be sterilely filtered and prepared for packaging and shipment.

The choice of processing steps at which the microdispersion treatment according to the present invention may be conducted in this hypothetical example depends on the presence of additives in the protein and the relative concentration

and volume of the protein. For example, most of the steps of the process diagrammed in FIG. 3 and described above would either contain very high concentrations of the material, or contain additives that would scatter or absorb the emission energy, thereby making them impractical for the microdispersion treatment process of the current invention. However, at Step 6" of the hypothetical process, no energy absorbing additives would be present in the protein solution and the average protein concentration of the IGI is only ~18mg/ml in an average solution volume of ~1200L. Although the overall volume would be large, because the concentration of the IGI protein would be low, the level of emission could be decreased and the exposure time could be decreased, while simultaneously allowing for an increase in the droplet size, thereby allowing for very high volume throughput for the microdispersion treatment device.

In contrast, the alternative hypothetical process in which the IGI protein would be treated at Step 2' would require significantly more vigorous treatment conditions. Here, while no emission absorbing additives would be present in the protein solution and while the total volume of the IGI would be only ~390L, the concentration of the IGI would be ~63mg/ml. Because the concentration of the protein would be high, if the microdispersion treatment is utilized at this stage of the hypothetical process, it would be necessary to run the emitter **12** at higher intensity, and/or provide for longer exposure times of the protein in the treatment chamber **16**, and/or create smaller droplet diameters to ensure that sufficient emission exposure is delivered to the entire volume of the protein material.

Although the above discussion describes a process involving the treatment of a protein, it should be understood that biological material or biochemically labile material is meant to encompass any material designed to be administered to a patient by any of several routes, including, but not limited to, intravenous or intramuscular injection, to provide a pharmaceutical effect, such as, for example, proteins, pharmaceuticals, gene therapy products, etc.

While the invention herein disclosed has been described by means of specific embodiments and applications thereof, numerous modifications and variations could be made thereto by those skilled in the art without departing from the scope of the invention set forth in the claims.